

## CLAIMS

1. Oligoclonal antibodies able to recognize and bind the antigenic epitope of at least one isoform of **human** clusterin in a selective and specific way, said epitope being **immunogenic and** characterised by a length from 10 to 20 amminoacids.

2. Oligoclonal antibodies according to claim 1, wherein said isoform is a glycosilated cytoplasmic or a non-glycosilated nuclear isoform.

3. Oligoclonal antibodies according to anyone of the claims 1 and 2, wherein the antigenic epitope of the non-glycosilated nuclear isoform comprises one of the following amminoacidic sequences: QFNWVSRLANLTQGEDQK (SEQ ID No 1); TKLKELPGVCNETMMALWEE (SEQ ID No 2) and derivatives thereof.

4. Oligoclonal antibodies according to anyone of claims 1 and 2, wherein the antigenic epitope of the glycosilated cytoplasmic isoform comprises one of the following amminoacidic sequences: TKLKELPGVCNETMMALWEE (SEQ ID No 2); TNEERKTLLSNLEEAQ (SEQ ID No 3); METVAEKALQEYRKK (SEQ ID No 4) and derivatives thereof.

5. Oligoclonal antibodies according to anyone of claims 1 to 4, wherein the antibodies are tagged.

6. Oligoclonal antibodies according to claim 5, wherein the antibodies are tagged with a fluorochrome, a radioactive isotope, an enzyme, biotin or a chemiluminescent substance.

7. Oligoclonal antibodies according to claim 6, wherein the fluorochrome is selected from the group consisting of fluoresceine, ficoeritrine, rodamine, texas red, cumarine.

8. Oligoclonal antibodies according to claim 6, wherein the radioactive isotope is  $^{14}\text{C}$  or  $^3\text{H}$ .

9. Oligoclonal antibodies according to claim 6, wherein the chemiluminescent substance is luciferin.

10. Oligoclonal antibodies according to claim 6, wherein the enzyme is selected from the group consisting of horseradish peroxidase (HRP) or alkaline phosphatase.

11. **Immunogenic** antigenic epitopes of at least one **human** clusterin isoform comprising at least one of the following

amminoacidic sequences: QFNWVSRLANLTQGEDQK (SEQ ID No 1); TKLKELPGVCNETMMALWEE (SEQ ID No 2); TNEERKTLLSNLEEAK (SEQ ID No 3); METVAEKALQEYRKK (SEQ ID No 4) and derivatives thereof.

5                   12. A method for the preparation of the oligoclonal antibodies, as defined in claims 1 to 10, which comprises the following steps:

                  solid phase synthesis of at least one of the antigenic epitopes as described in claim 11;

10                   conjugation of at least one of the antigenic epitopes wherein a proteic carrier in order to make the epitope immunogenic;

                  animal immunization with this immunogenic epitope in complete Freund adjuvant;

15                   serum withdrawal from this animal and purification of the oligoclonal antibodies.

                  13. A method according to claim 12, wherein the proteic carrier is the bovine serum albumin.

                  14. A method according to claims 12 and 13, wherein the animal is rabbit.

20                   15. An immunological method for detection of the clusterin levels in biological samples which comprises the following steps:

                  protein extraction from this biological sample;

25                   specific incubation of the proteic extract with at least one of the oligoclonal antibodies described in claims 1 to 10, in order to obtain an antigen-antibody complex;

                  qualitative and quantitative revelation of the antigen-antibody complex.

                  16. Immunological method according to claim 15 for tumours diagnosis and the prediction of their malignancy grade.

30                   17. An immunological method according to claim 15, wherein the biological sample is selected from the group consisting of blood, stool, seminal fluid, pleural fluid, ascitic fluid, urine, liquor.

35                   18. An immunological method according to anyone of claims 15 and 17, wherein the tumours are colorectal, breast, prostate, testis and ovary carcinomas, tumours of the Central Nervous System and of the haemo-lymphopoietic system.

19. An immunological method according to anyone of claims 15 to 18, wherein the detection of step c) is done by using one of the following techniques: ELISA, Western Blot, RIA, immunohistochemistry.

5                   20. Diagnostic kit for tumours diagnosis and prediction of their malignancy grade which comprises at least one of the oligoclonal antibodies as defined in claims 1 to 10.

10                   21. Diagnostic kit according to claim 19, wherein the tumours are colorectal, breast, prostate, testis and ovary carcinomas, tumours of the Central Nervous System and of the haemo-lymphopoietic system.

15                   22. Use of at least one of the oligoclonal antibodies defined in claims 1 to 10, for qualitative and quantitative determination of at least one **human** clusterin isoform levels in a biological sample.

20                   23. Use according to claim 22 for tumour diagnosis and the prediction of its malignancy grade.

25                   24. Use according to claim 22, wherein the qualitative and quantitative determination is carried out through one of the following techniques: ELISA, RIA, immunohistochemistry, Western Blot.

30                   25. Use according to anyone of claims 22 and 24, wherein the tumours are selected from the group consisting of colorectal, breast, prostate, testis and ovary carcinomas, tumours of the Central Nervous System and of the haemo-lymphopoietic system.

35                   26. Use according to anyone of claims 22 to 25, wherein the biological sample is selected from the group consisting of blood, stool, seminal fluid, pleural fluid, ascitic fluid, urine, liquor."

## SUMMARY

The invention concerns anti-clusterin oligoclonal antibodies able to recognize and bind in a selective and specific way antigenic epitopes of clusterin isoforms to be used in tumours diagnosis and in the prediction of their malignancy grade, diagnostic method and related kits.

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